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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/322,732 | 05/28/1999 | KEITH R. MAROTTI | PUJ-0041 | 8413 |

34135 7590 11/26/2003

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| EXAMINER | |
|---|---|
| ROBINSON, HOPE A | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1653 | |

DATE MAILED: 11/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/322,732 | MAROTTI ET AL. | |
| | Examiner | Art Unit | |
| | Hope A. Robinson | 1653 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *11 August 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *4-8,15-18 and 140-150* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *4-8,15-18 and 140-150* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. §§ 119 and 120**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 11, 2003 has been entered.

2. Applicant's response to the Office Action mailed July 10, 2003 on August 11, 2003 is acknowledged.

3. Claims 1-3, 9-14 and 19-139 have been canceled. Claims 4-8, 15-18 and 140-150 have been amended. Claims 4-8, 15-18 and 140-150 are pending and are under examination.

4. The following objection and rejection is or remains applicable:

### *Specification*

The specification is objected to because of the following incorrect sentence structure: "The identification of compounds that compete with the binding of radio-labeled oxazolidinones to 50S or 70S bacterial ribosomes and inhibit the formation of the translation initiation complex" which is a dangling participle.

5. The amendment filed August 11, 2003 is objected to under 35 U.S.C. 132 because the amendment introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: claims 4, 5, 142 and 143 have been amended to recite "wherein an increase in said intrinsic fluorescence of efp indicates that said compound increases said activity" and "wherein a decrease in said intrinsic fluorescence of efp indicates that said compound decreases said activity" and there is no support for this in the instant specification. The specification on page 15 indicates that the claimed invention determines "whether the compound binds to efp can also be accomplished by measuring the intrinsic fluorescence of efp and determining whether the intrinsic fluorescence is modulated in the presence of the compound". The specification also reports that a "decrease in fluorescence intensity indicates binding of the compound to efp". On page 18 it is stated that the intrinsic fluorescence of efp is measured as function of changes in the fluorescence of the tryptophan residue(s) of efp. Page 26 of the specification provides a formula for calculating fluorescence intensity. Therefore, there is no support in the instant specification for the conclusion drawn that an increase in intrinsic fluorescence of efp results in an increase in efp activity.

Applicant is required to cancel the new matter in the reply to this office action.

***Claim Rejections - 35 U.S.C. § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 4-8, 15-18 and 140-150 rejected under 35 U.S.C. 112 first paragraph, because the specification while being enabled for a binding assay, does not reasonable provide enablement for the full scope of the claims, for example a method for identifying a compound (unspecified) that increases an activity of efp (unspecified) by contacting efp with a compound (unspecified). The specification is enabled for a binding assay using radiolabeled oxazolidinone bound to efp (such as linezolid or eperezolid) see pages 15+ of the specification. However, the specification is not enabled for a method with an unspecified amount of compounds or a method to identify compounds that increase any or all activity of efp per se as the specification does not exemplify such a method. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. These factors include, but are not limited to: quantity of experimentation necessary, amount of direction or guidance presented, presence or absence of working examples, nature of the invention, state of the prior art, relative skill of those in the art, predictability or unpredictability of the art and breath of the claims, these factors are addressed below.

The claimed invention is directed to a method which encompasses any and all possible compounds and a method step that utilizes the unidentified compound in the process and a method that does not identity the specific efp activity that is to be increased or the nexus between fluorescence and increased activity. The methods

recited in the claims provides no indicia how you can go from a preamble of identifying a compound that increase efp activity and result in an increase in L16 protein activity. Note that the methods recited in claims 6-8, 15-18 and 144-150 do not provide any method step as to how the efp activity will increase as a result of contacting the unknown compound with efp. Note that the claimed method appears to be a binding assay although not disclosed as such. Further, the specification provides only examples and no specific assays to accompany the claimed method. The specification asserts that contacting can take place in buffers or media well known to those skilled in the art. It is also stated that varying amounts of the test compound can be used as desired by the practitioner. Thus, it appears that much of the parameters involved in the method can be adjusted arbitrarily which invites one skilled in the art to perform undue experimentation, absent specific guidance.

Additionally, the specification asserts that the claimed method will identify a compound that modulates the activity of prokaryotic efp, determine whether the compound modifies activity of efp, for example determining if the compound binds to efp by a number of art recognized procedures (i.e. binding assays such as a gel-shift mobility electrophoresis, Western blot, filter binding and scintillation proximity assay). Note that the claimed method is relying on art recognized procedures, yet the specification asserts that this is a new method/procedure. It is also possible for a compound to bind to efp and not produce an effect thus applicant need to provide specific detail regarding the method steps and not rely on the general skill and knowledge in the art. Thus the information provided in the specification is exemplary and not limiting, therefore, does not breathe life into the claims.

In view of the foregoing, one skilled in the art would have to engage in undue experimentation to be able to practice the full scope of the claims since the specification

does not provide sufficient detail. In the absence of sufficient guidance/direction regarding the steps to determine whether the test compound modulates the activity of efp one skilled in the art would not be able to practice the claimed invention commensurate in scope with the claims. Further, the claimed methods do not have endpoints/results that correspond with the preamble of the claims, thus, it doesn't appear that the objective of the method is obtained. In fact the claims read on a binding assay rather than a method to identify a compound that has the desired effect on efp, however, there is no specific assay and measurements to obtain this information nor information as to whether modulation is up or down (see for example claim 14). Note for example that the prior art teaches that genes encoding certain ribosomal proteins can be deleted from the chromosome without an apparent effect on cell viability. It is also stated that most initiation, elongation and termination factors are required for cellular growth, however, some of these proteins may be dispensable under certain growth conditions (Aoki, et al., The Journal of Biological Chemistry, vol. 272, no. 51, 1997). In view of the prior art the specification needs to provide guidance as to how the compound is determined, what the compound is, how the efp activity will be modulated, what effect the modulation will have on the function of the efp and a specific assay and measurement steps to achieve all of the above. The claims should state how a preamble to increase efp activity results in an end point of increased activity of a L16 protein.

Absent exemplification of a specific assay to assay a specific compound the specification is not enabled for a method that modulates an activity of efp. Further, since no guidance or direction is provided regarding the determination of the test compound it would require undue experimentation to be able to practice the claimed invention. It is noted that applicant provides a formula to calculate the fluorescence

intensity on page 26, however not all the variables have been explained for example, it is unclear what the variable *iXI* represents. Note also that the calculation of micro Molar oxazolidinone is incorrect as the specification reports 42 micro Molar, which should be 41.1 micro Molar. The specification also states that a correction for the inner filter effect of the drug (oxaxolidinones) is necessary, however, it is unclear how this is done as the specification provides no guidance/direction to perform this.

Thus, for all of the above reasons, the specification is not considered to be enabling without undue experimentation, because, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to enable one skilled in the art to be able to practice the invention commensurate in scope with these claims.

7. Claims 4, 5, 142 and 143 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claimed invention is directed to a method for identifying a compound that decreases or increases an activity of prokaryotic elongation factor p (efp). The claims recite the following added material which is not supported by the original disclosure: claims 4, 5, 142 and 143 have been amended to recite "wherein an increase in said intrinsic fluorescence of efp indicates that said compound increases said activity" and "wherein an decrease in said intrinsic fluorescence of efp indicates that said compound decreases said activity" and there is no support for this in the instant specification. The specification on page 15 indicates that the claimed invention determines "whether the compound binds to efp can

can also be accomplished by measuring the intrinsic fluorescence of efp and determining whether the intrinsic fluorescence is modulated in the presence of the compound". The specification also reports that a "decrease in fluorescence intensity indicates binding of the compound to efp". On page 18 it is stated that the intrinsic fluorescence of efp is measured as function of changes in the fluorescence of the tryptophan residue(s) of efp. Page 26 of the specification provides a formula for calculating fluorescence intensity. Therefore, there is no support in the instant specification for the conclusion drawn that an increase in intrinsic fluorescence of efp results in an increase in efp activity.

Thus, it is apparent that the specification lacks sufficient guidance/written description for one of skill in the art to be able to practice the claimed invention without performing undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

8. Claims 4-8, 15-18 and 140-150 remain rejected under 35 U.S.C. 112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 remain indefinite because the claim recites "a method for identifying a compound that increases an activity of a prokaryotic elongation factor p (efp)" and it is unclear what activity of efp is being increased and there is no nexus between fluorescence and increase in activity (see also claims 5 and 142-143).

Claim 5 is indefinite because the claim does not recite a period at the end of the sentence.

Claim 6 is indefinite because the claim is missing some essential steps for example how to determine whether the compound (unspecified) is measured to determine increase in activity (unspecified).

Claim 7 is indefinite because the claim recites a "method to identify a compound that increases an activity of prokaryotic elongation factor p" and there is no indication of how contacting a compound with efp results in an increase in activity especially since the compound is unknown. The claim is also indefinite because step (c) is determining whether said compound that increases the activity of efp and a L16 protein, yet the preamble of the claim is to identify a compound increasing efp activity (see also claims 144-145).

Claim 8 is indefinite because the claim recites a method to identify a compound that increases an activity of efp, however, no indication is given as to what activity and the claim is measuring binding of an unspecified compound to efp and no correlation is made between binding and an increase an efp activity. See also claims 15-18 sand 146-150 that have the same claim language.

Claims 140-141 are indefinite because the claims recite a method that modulates the activity of a L16 protein, however, the claim does not recite whether modulation is upward or downward. The claim is also indefinite as to the recitation of the L16 protein being in "association" with efp. What is this association?

9. Applicant's response filed August 11, 2003 has been considered, however, the rejections of record remains because the arguments presented were not persuasive. Pages 10-11 of the response states that no undue burden exists and that there is no

reason to doubt the objective truth of the statements contained in the application. That the present application is drawn to methods of screening compounds that modulate efp. These arguments are not persuasive because: 1) the claims are directed to methods of identifying a compound that increases efp activity (claims 4-8, 15-18 and 142-150) or methods of modulating an activity of L16 (claims 140-141), thus there are no claims directed to a method of screening for a compound that modulate efp; 2) the claims recite a preamble that results in a different end product for example claims drawn to increasing efp activity but result in increasing the activity of L16; the methods do not indicate what activity of efp is being increased and one of skill in the art would not know activity to monitor and there is no support in the specification for an increase of all efp activities; 3) there is no indication of how the fluorescence measured results in increased efp activity and 4) some claims do not require binding of the compound to efp to produce an effect of increased activity. Undue burden is evident.

Applicant on pages 12-15 argues that it is not necessary to specify what activity of efp is being increased because "one potential effect of decreasing the activity of efp is to identify compounds that can decrease cell viability". Note that applicant is offering a potential outcome not an actual outcome. Note also that page 2 of the specification discloses that efp stimulates efficiency of the peptidyltransferase activity of prokaryotic ribosomes and modulates the efficiency of protein synthesis. Neither the claim or the specification indicates what specific activity the compound is going to alter, will it increase the protein synthesis activity of efp? Are all efp activity increased? Some of the methods disclosed merely determines if binding occurs see for example claim 4 and applicant states on page 15 of the response that one can calculate the degree of which the test compound can bind to efp, which signifies a binding assay not the methods as claimed. Specific not general teaching is required and adequate guidance

to practice the claimed invention commensurate in scope with the claims. Therefore, for these reasons and those stated above the rejections remain. Note that new grounds of rejections have been instituted based on applicant's amendments to the claims.

***Conclusion***

10. No claims are presently allowable.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Hope A. Robinson whose telephone number is (703)308-6231. The Examiner can normally be reached on Monday - Friday from 9:00 A.M. to 6:30 P.M. (EST).

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor Christopher S.F. Low, can be reached at (703)308-2932.

Any inquiries of a general nature relating to this application should be directed to the Group Receptionist whose telephone number is (703)308-0196.

Papers related to this application may be submitted by facsimile transmission. The official fax phone number for Technology Center 1600 is (703) 308-2742. Please affix the Examiner's name on a cover sheet attached to your communication should you choose to fax your response. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989).

Hope A. Robinson, MS

Patent Examiner

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